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UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

CHARLES H. **HANNUM**,
JANICE A. CULPEPPER, FRANK D. LEE, and DANIEL BIRNBAUM
(08/472,168 and 08/484,882),
Junior Party,

v.

IMMUNEX CORPORATION
(09/983,806 and 10/095,449),
Senior Party.

Interference No. 105,099

Before SCHAFER, TORCZON, and LANE, Administrative Patent Judges.

TORCZON, Administrative Patent Judge.

JUDGMENT ON HANNUM PRELIMINARY MOTION 1
(PURSUANT TO 37 CFR § 1.640)

INTRODUCTION

Hannum has filed Hannum preliminary motion 1 for judgment of no interference-in-fact (Paper 23). Immunex neither joins nor opposes the motion (Paper 24). We GRANT Hannum preliminary motion 1.

FINDINGS SUPPORTED BY A PREPONDERANCE OF THE EVIDENCE

[1] The interference involves a ligand for flt3, a tyrosine kinase receptor involved in hematopoietic cell proliferation and differentiation. The ligand regulates the growth and differentiation of hematopoietic progenitor and stem cells.[1]

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[1] S.D. Lyman & M.P. Beckmann, "Ligands for flt3 receptors", U.S. 2002/0107365 A1 at "Background of the invention" (8 Aug. 2002) (the patent application publication for Immunex's involved 806 application) [hereinafter exhibit 3001].

[2] According to Immunex,[2] flt3-ligand ("flt3-L")

> refers to a genus of polypeptides that bind and complex independently with flt3 receptor found on progenitor and stem cells. The term "flt3-L" encompasses proteins having the amino acid sequence 1 to 231 of SEQ ID NO:2 or the amino acid sequence 1 to 235 of SEQ ID NO:6, as well as those proteins having a high degree of similarity or a high degree of identity with the amino acid sequence 1 to 231 of SEQ ID NO:2 or the amino acid sequence 1 to 235 of SEQ ID NO:6, and which proteins are biologically active and bind the flt3 receptor. In addition, the term refers to biologically active gene products of the DNA of SEQ ID NO:1 or SEQ ID NO:5. Further encompassed by the term "flt3-L" are the membrane-bound proteins (which include an intracellular region, a membrane region, and an extracellular region), and soluble or truncated proteins which comprise primarily the extracellular portion of the protein, retain biological activity and are capable of being secreted. Specific examples of such soluble proteins are those comprising the sequence of amino acids 28-163 of SEQ ID NO:2 and amino acids 28-160 of SEQ ID NO:6.

[3] Count 1, the sole count, is (Paper 1[3] at 4):

> A polypeptide of Immunex 806 claim 49.

[4] Immunex 806 claim 49 is [2003]:[4]

> An isolated polypeptide that binds to flt3, wherein said polypeptide comprises amino acids 28-163 of SEQ ID NO:2.

[5] Immunex SEQ ID NO:2 is a 231-residue polypeptide [2001].

[6] All of the claims of both parties correspond to the count (Paper 1 at 4):

> Hannum 168 claims 54-74
>
> Hannum 882 claims 28-30
>
> Immunex 806 claims 49-58

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[2] 3001 at ¶0026.

[3] Notice Declaring Interference. Hannum has provided a copy of the declaration [2002]. The filing of duplicate papers is discouraged (Paper 2, Standing Order, at § 12).

[4] Hannum exhibits are numbered from 2001.

Immunex 449 claims 1-15

[7] The Immunex 806 claims and the Hannum 882 claims are drawn to flt-ligand polypeptides [2003; 2005].

[8] The Immunex 449 claims and the Hannum 168 claims are drawn to antibodies (or kits using such antibodies) for the flt3 ligand as each party has claimed the ligand [2004; 2006].

[9] The Immunex claims all define the claimed invention in terms of relatively long subsequences of Immunex SEQ ID NO:2.[5]

[10] The Hannum claims are generic to the Immunex claims in the sense that they recite properties of the defining flt3-ligand polypeptide, including relatively short subsequences, rather than reciting a continuous, relatively large subsequence as Immunex does (e.g., Paper 22, unopp'd facts 10 and 18).

[11] The Immunex species claims defined by its SEQ ID NO:2 anticipate Hannum's generic claims.[6]

[12] According to Hannum, nothing in its claims or specification teach or suggest the specific polypeptide sequence of Immunex SEQ ID NO:2, which is central to the definition of the Immunex invention in the involved Immunex claims (e.g., Paper 22, unopp'd facts 17 and 20).

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[5] Immunex 806 claims 52 and 56 and 449 claims 1, 6, and 11 are defined in terms of a deposited vector, but neither party has argued that this vector represents a sequence different from the relevant portions of Immunex SEQ ID NO:2.

[6] The Hannum kit claims would not be anticipated, but their separate patentability has not been separately argued. Presumably Hannum concedes for the purpose of this motion that the use of antibodies to a known polypeptide in the form of a kit is too obvious to contest.

[13] Consequently, according to Hannum, the two-way test for an interference-in-fact fails because Hannum's claimed invention would not bar issuance (i.e., would not have anticipated or rendered obvious the subject matter of) Immunex's claims.

[14] The examiners who proposed the interference were consulted. They replied:

> Both applications describe the isolation of the mouse Flt3 ligand which binds to Flt3, a receptor found on hematopoietic cells, and stimulates proliferation of those cells. Although the claims of the two applications claim the protein differently, Hannum by physical properties and partial sequence, and [Immunex] by amino acid sequence alone, the proteins are from the same organism and have the same activity, and the partial sequences of Hannum et al. are comprised in the complete sequence of [Immunex]. Immunex [sic, Hannum's] argument that Hannum has three "isoforms" of the protein is not supported by fact. Rather, it appears that Hannum had three partial or preliminary clones, which do not necessarily represent different forms in vivo. Rather, the person of ordinary skill in the art, given Hannum's three sequences, would derive a consensus sequence from them, likely to represent the actual protein. Hence, as Hannum actually had the mouse protein in hand and determined its physical properties and activity, in the express absence of evidence to the contrary, it is presumed that the protein of Hannum is identical to that of Immunex, and that the amino acid sequence, which is an inherent property of the protein, is also identical. Therefore, the claims of Immunex would be held to be anticipated by Hannum.
>
> To overcome a 102 rejection as set forth above, the burden would be on Immunex to show fact or evidence that their protein did, in fact, differ from that isolated by Hannum et al. The mere presence of three sequences in Hannum's specification is not sufficient to establish this.

[15] Representative Hannum 882 claim 28 claims the invention as follows [2005]:

> A substantially pure naturally occurring mammalian Flt3 ligand protein which binds to a Flt3 receptor, wherein said protein has the following physical characteristics:
>
> a) said protein migrates as an approximately 30 KD glycoprotein on SDS-Polyacrylamide gel electrophoresis under reducing conditions;

b) said protein precipitates in ammonium sulfate at 60 to 85% saturation at 4°C;

c) on hydrophobic interaction chromatography with an $(NH_4)_2SO_4$ gradient in 20mM Tris, pH 7.5, on a Phenyl-5PW column, said protein elutes between 900-750 [sic] mM $(NH_4)_2SO_4$;

d) on anion exchange chromatography (NaCl gradient in 20 mM Tris, pH 7.5 on Mono Q column), said protein elutes between 130-250 mM NaCl;

e) on cation exchange chromatography (NaCl gradient in 10 mM citrate, pH 3.0 on Mono S column), said protein elutes between 440-540 mM NaCl;

f) on gel filtration chromatography (Sephacryl S200 column), said protein runs with an apparent molecular weight of 70 kD;

g) on reversed phase HPLC (water to acetonitrile gradient in 0.1% TFA on a Poros R/H column), said protein elutes between 32-35% acetonitrile; and

h) said protein comprises a sequence selected from the group consisting of:

i) Phe Val Gln Thr Asn Ile Ser His Leu Leu Lys (SEQ. ID No. 1);

ii) Asp Tyr Pro Val Thr Val Ala Val Xaa Leu Gln Asp Glu (Residues 1-13 of SEQ. ID No. 2); and,

iii) Trp Ile Glu Gln Leu Lys (Residues 1-6 of SEQ. ID No. 4).

[16] Hannum SEQ ID NO:1 is [3002]:[7]

Phe Val Gln Thr Xaa Ile Ser His Leu Leu Lys

[7] C.H. Hannum, J.A. Culpepper, F.D. Lee & D. Birnbaum, "Purified Mammalian Flt3 Ligands; Agonists; Antagonists", Appln. No. 08/484,882 (filed 7 June 1995).

[17] The disclosed sequence and the claimed sequence differ by the substitution of "Asn" (asparagine) in the claimed sequence for "Xaa" (unknown or other) in the disclosed sequence.

[18] Hannum SEQ ID NO:2 is [3002]:

Asp Tyr Pro Val Thr Val Ala Val Asn Leu Gln Asp Glu Lys

[19] The disclosed sequence and the claimed partial sequence differ by the substitution of "Xaa" (unknown or other) in the claimed sequence for "Asn" (asparagine) in the disclosed sequence. As indicated in the claim, the fourteenth disclosed amino acid residue "Lys" is not included in the claimed partial sequence.

[20] Hannum SEQ ID NO:4 is [3002]:

Trp Ile Glu Gln Leu Lys Gln Pro Gly Ser

[21] As indicated in the claim, the last four disclosed amino acid residues "Gln Pro Gly Ser" are not included in the claimed partial sequence.

[22] The Hannum claimed sequences (in bold) match against Immunex SEQ ID NO:2[8] as follows:

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Immunex:      MTVLAPAWSPNSSLLLLLLLLSPCLRGTPDCYFSHSPISS     40

Immunex:      NFKVKFRELTDHLLKDYPVTVAVNLQDEKHCKALWSLFLA     80
SEQ ID NO:2:  ..............DYPVTVAVXLQDE.............

Immunex:      QRWIEQLKTVAGSKMQTLLEDVNTEIHFVTSCTFQPLPEC    120
SEQ ID NO:4:  ..WIEQLK................................

Immunex:      LRFVQTNISHLLKDTCTQLLALKPCIFKACQNFSRCLEVQ    160
SEQ ID NO:1:  ..FVQTNISHLLK............................

Immunex:      CQPDSSTLLPPRSPIALEATELPEPRPRQLLLLLLLLPLT    200
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[8] Each translated into the standard single-letter code for amino acids for easier comparison.

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Immunex:      LVLLAAAWGLRWQRARRRGELHPGVPLPSHP          231
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[23] The Hannum claimed subsequences are identically contained within Immunex SEQ ID NO:2, and within the range specified in the count (28-163) provided the unknown ("X") in Hannum SEQ ID NO:2 is asparagine ("N") as Hannum discloses in its specification.

[24] Neither party appears to be contending that the invention of Immunex 806 claim 49, which is based on Immunex SEQ ID NO:2, anticipates the invention of Hannum 882 claim 28. From this, we infer that the non-sequence physical characteristics recited in Hannum's claim are met by flt3 ligands with sequences similar to Immunex SEQ ID NO:2.

[25] The Hannum claimed subsequences are consensus sequences that appear to be based on murine (mouse) isoforms of flt3 ligand [3002 at 8:32-11:38].

[26] Immunex SEQ ID NO:2 is a murine sequence [e.g., 3001 at 0050].

[27] Hannum discloses three separate murine flt3 ligand isoforms (MoT118,[9] MoT110,[10] and MB8) and two human isoforms (HuS86 and HuS109). The murine isoforms match against Immunex SEQ ID NO:2 as follows (where "." indicates a gap, bold indicates a difference, and underlining indicates the Hannum claimed subsequences):

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Immunex:   MTVLAPAWSPNSSLLLLLLLLSPCLRGTPDCYFSHSPISS     40
MoT118:    MTVLAPAWSPNSSLLLLLLLLSPCLRGTPDCYFSHSPISS     40
MoT110:    MTVLAPAWSPNSSLLLLLLLLSPCLRGTPDCYFSHSPISS     40
MB8:       MTVLAPAWSPNSSLLLLLLLLSPCLRGTPDCYFSHSPISS     40
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[9] Hannum SEQ ID NO:40.

[10] Hannum SEQ ID NO:38

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Immunex:  NFKVKFRELTDHLLKDYPVTVAVNLQDEKHCKAL......    74
MoT118:   NFKVKFRELTDHLLKDYPVTVAVNLQDEKHCKAL......    74
MoT110:   NFKVKFRELTDHLLKDYPVTVAVNLQDEKHCKAL......    74
MB8:      NFKVKFRELTDHLLKDYPVTVAVNLQDEKHCKALDRVSLL    80

Immunex:  ......................WSLFLAQRWIEQLKTVA    91
MoT118:   ......................WSLFLAQRWIEQLKTVA    91
MoT110:   ......................WSLFLAQRWIEQLKTVA    91
MB8:      CRLGLTLNSLQSSCLSVLSAGITWSLFLAQRWIEQLKTVA   120

Immunex:  GSKMQTLLEDVNTEIHFVTSCTFQPLPECLRFVQTNISHL   131
MoT118:   GSKMQTLLEDVNTEIHFVTSCTFQPLPECLRFVQTNISHL   131
MoT110:   GSKMQTLLEDVNTEIHFVTSCTFQPLPECLRFVQTNISHL   131
MB8:      GSKMQTLLEDVNTEIHFVTSCTFQPLPECLRFVQTNISHL   160

Immunex:  LKDTCTQLLALKPCIFKACQNFSRCLEVQCQPDSSTLLPP   171
MoT118:   LKDTCTQLLALKPCIFKACQNFSRCLEVQCQPGNGGPRAQ   171
MoT110:   LKDTCTQLLALKPCIFKACQNFSRCLEVQCQPDSSTLLPP   171
MB8:      LKDTCTQLLALKPCIFKACQNFSRCLEVQCQPDSSTLLPP   200

Immunex:  RSPIALEATELPEPRPRQLLLLLLLL.PLTLVLLAAAWGL   210
MoT118:   HHGATRLTATALLTVCPGLLLPLVGT.SHMFFLPYFLSFL   210
MoT110:   RSPIALEATELPEPRPRQLLLLLLLLLPLTLVLLAAAWGL   211
MB8:      RSPIALEATELPEPRPRQLLLLLLLLLPLTLVLLAAAWGL   240

Immunex:  RWQRARRRGELHPGVPLPSHP                     231
MoT118:   SSFLKMYLYV...........                     220
MoT110:   RWQRARRRGELHPGVPLPSHP                     232
MB8:      RWQRARRRGELHPGVPLPSHP                     261
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[28] The examiner argues that a consensus sequence between the three Immunex isoforms would yield Immunex SEQ ID NO:2. If we ignore MB8 as simply a variant of MoT110, it is not clear how one skilled in the art would choose a consensus sequence between the two isoforms. Alternatively, if MB8 is considered, the simplest consensus sequence (majority rule at each differing position, gaps permitted) would yield the MoT110 sequence, which differs from Immunex SEQ ID NO:2 by the addition of a leucine residue at position 198.

[29] It is conceivable that additional experimentation would have led to a convergence on a consensus sequence identical to Immunex SEQ ID NO:2. The misreading of an additional leucine residue after a string of eight leucine residues is well within the realm of the possible. Such possibilities are not sufficient to support a determination that Immunex SEQ ID NO:2 is inherent in the flt3 ligand genus Hannum claims.

DISCUSSION

A movant seeking judgment of no interference-in-fact must establish that the parties' involved claims are patentably distinct. Nitz v. Ehrenreich, 537 F.2d 539, 190 USPQ 413 (CCPA 1976); Case v. CPC Int'l, Inc., 730 F.2d 745, 750, 221 USPQ 196, 200 (Fed. Cir. 1984).[11] In the present interference Hannum, the junior party, seeks to establish that its invention, as represented in its claims, would not have anticipated or rendered obvious the subject matter of the involved Immunex claims.[12]

The position of the United States Patent and Trademark Office is that Hannum's generic claim inherently describes the invention that Immunex claims. An inherency argument, however, may not be established by probabilities or possibilities. The fact that a result may occur in a specific set of circumstances is not sufficient. MEHL/Biophile Int'l Corp. v. Milgraum, 192 F.3d 1362, 1365, 52 USPQ2d 1303, 1305

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[11] At the risk of seeming pedantic, we feel it worth noting that interference-in-fact and no interference-in-fact are opposite sides of the same coin. While it is proper to talk about a "two-way" patentability test for whether an interference-in-fact exists, the question formally before us is whether no interference-in-fact exists. A two-way test for interference-in-fact is required precisely because the test for no interference-in-fact is a one-way test: two-ways to get in is necessary because one-way is sufficient to get out. Notice, "Standard for Declaring an Interference", 65 Fed. Reg. 79809, 79810 (Dir., USPTO 20 Dec. 2000).

[12] This approach is not without risk to Hannum because it leaves open the possibility that Hannum's claims are anticipated or obvious in view of the published Immunex applications based on 35 U.S.C. 102(e) rather than § 102(g), which is the basis for this interference.

(Fed. Cir. 1999). The existence of three isoforms that are markedly distinct from each other as well as from Immunex SEQ ID NO:2 militates against a finding that the flt3 ligand species of Immunex is inherent in Hannum's generic description of its claimed flt3 ligands. Taken at face value, it is possible to isolate many flt3 ligands from mice that are sequentially distinct from Immunex SEQ ID NO:2. There is no more than a speculative basis for inferring that further experimentation would have lead to a convergence of what Hannum discovered and what Immunex claims.

The examiner relies on an In re Best, 562 F.2d 1252, 1254-55, 195 USPQ 430, 433-34 (CCPA 1977), approach to support a finding of inherency. Best, however, is distinguishable from the present case on both facts and procedure. Best claimed a zeolite in terms of its physical characteristics and a process for making the zeolite in functional language directed at a property of the finished product. The examiner rejected the claims over prior art showing a very similar process for making a zeolite, but lacking a description of the functional step of the process. The court concurred that the examiner had made out a prima facie case of inherency sufficient to shift the burden to Best to prove a difference. Cf. In re King, 801 F.2d 1324, 1327, 231 USPQ 136, 139 (Fed. Cir. 1986) (the Office is not equipped to test the properties of claimed inventions against prior art). The problem here is that the face of the Hannum specification undermines the prima facie case of inherency by providing exceptions to any inherency finding. The speculation that further investigation might produce a different result cannot overcome this problem.

The procedural distinction lies in the fact that Best and King arise in the context of ex parte examinations rather than interference proceedings. The observation that the Office is not equipped to test theories, while certainly true, does not extend to parties in an interference, who are obligated to provide positive proof or live with the consequences of failing to do so.[13]

An interference is, by nature, a provisional rejection of each party's involved claims over the claims of the other party under 35 U.S.C. 102(g). The contested rejection is the rejection of the Immunex claims over the Hannum claims. The examiner is correct that, ex parte, a burden could shift to Immunex to show why Hannum's invention does not anticipate the Immunex claims. In an interference, however, the burden lies with the movant, 37 C.F.R. § 1.637(a), which is Hannum, not Immunex. Hannum, the putative reference, insists that it does not anticipate or render obvious the subject matter of the Immunex claims. The evidence of record supports Hannum's position so Hannum is under no additional burden to prove its point experimentally. Instead, the burden has shifted to Immunex to disprove Hannum's contention. Immunex has declined to do so. Both sides must live with the consequences of their actions and inactions. 37 C.F.R. § 1.658(c). Neither will be able to provoke an interference with the other on this subject matter at a later date. Hannum will not be able to rely on any proofs it may have to the Immunex isoform of flt3 ligand in an

[13] This is not to say that a Best-like situation could not arise in an interference. For instance, when the Board raises a question of patentability under 37 C.F.R. § 1.641, the proceeding may be in the nature of an ex parte examination, particularly when the unpatentability appears to apply to both parties such that there is no genuine adversity. This is not the case here. There is no evidence of a settlement or any other indication that the parties are not dealing at arms length.

antedating effort under 37 C.F.R. § 1.131. Other consequences may also become apparent.

In a priority contest, a party can always give up or settle away its claim to priority. Cf. 35 U.S.C. 135(c) and (d); 37 C.F.R. § 1.662. In moving for a judgment of no interference-in-fact, Hannum has given up on its opportunity to contest the priority of the species that Immunex is claiming. In failing to oppose, Immunex has surrendered what may be its best opportunity to avoid a dominating claim.

While the parties may be estopped from pursuing various remedies inside and outside the Office, the Office is not so estopped. Fundamentally, a priority contest is about who loses, not who wins. In re Kyrides, 159 F.2d 1019, 1022, 73 USPQ 61, 63 (CCPA 1947). A judgment of no interference-in-fact is not a mandate to the examiner to issue claims. Indeed, as indicated above, if the Immunex applications mature into patents, Hannum may well be subject to a rejection under § 102(e). In the absence of interfering subject matter, however, we cannot pursue that question here.

REHEARING

Since the motion is unopposed and results in a final decision, we proceed directly to judgment without issuing an order to show cause. Since both parties have had an opportunity to submit evidence, no additional testimony period would be set in any case. Consequently, if a party wishes to challenge this decision it may do so in the form of a request for reconsideration filed within 21 days of the date of this judgment.

ORDER

Upon consideration of Hannum Preliminary Motion 1, it is:

ORDERED that U.S. 2002/0107365 A1 be entered in the record as exhibit number 3001;

FURTHER ORDERED that the 08/484,882 application be entered in the record as exhibit number 3002;

FURTHER ORDERED that judgment be awarded to both parties on the basis that there is no interference-in-fact for the subject matter of Count 1;

FURTHER ORDERED that any request for rehearing be filed **within 21 days of the date of this judgment**; and

FURTHER ORDERED that a copy of this decision be entered in the administrative record of the Hannum 08/472,168 and 08/484,882 applications and the Immunex 09/983,806 and 10/095,449 applications.

RICHARD E. SCHAFER
Administrative Patent Judge

RICHARD TORCZON
Administrative Patent Judge

SALLY GARDNER LANE
Administrative Patent Judge

BOARD OF PATENT APPEALS AND INTERFERENCES

INTERFERENCE TRIAL SECTION

cc (electronic mail):

For Hannum (Schering Corp. and INSERM Institut National de la Santé et de la Recherche Médicale): **Steven W. Parmelee** and **Kevin L. Bastian** of TOWNSEND AND TOWNSEND AND CREW LLP.

For Immunex Corp. (a subsidiary of Amgen Inc.): **Gordon Kit** of SUGHRUE MION, PLLC and **Janis C. Henry** of AMGEN INC.

Notice: Any agreement or understanding between parties to this interference, including any collateral agreements referred to therein, made in connection with or in contemplation of the termination of the interference, shall be in writing and a true copy thereof filed in the United States Patent and Trademark Office before termination of the interference as between said parties to the agreement or understanding. 35 U.S.C. 135(c); 37 C.F.R. § 1.661.